Title

The Role of Education in Executive Functions, Behavioral Problems and Functional Performance in People with Schizophrenia.

Running title

Education, Cognitive Reserve & Schizophrenia

Authors

Silvia Cámara[1], Israel Contador[2*], Paula Herrero[3], Pablo Ruisoto[3], Abraham Sánchez[3], Luis Cuellar[4], Rebeca López[4], Mª Concepción Fournier[1], Francisco Ramos[5],

1. Children's University Hospital of Niño Jesús. Madrid, Spain.

2. Department of Basic Psychology, Psychobiology and Methodology of Behavioral Science. University of Salamanca, Salamanca, Spain.

3. Psychiatric Institute José Germain. Madrid, Spain.

4. Hospital Center Benito Menni, Valladolid, Spain.

5. Department of Personality, Assessment and Psychological Treatments. University of Salamanca, Salamanca, Spain.

***Author of correspondence**: Israel Contador. Facultad de Psicología, Universidad de Salamanca, Avda. de la Merced 109-131, ES-37005, Salamanca, Spain. E-mail: icontador@usal.es. Telephone number: +34923294500

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Abstract

Objective: This cross-sectional study examined the influence of education on executive functions, behavioral problems and functional performance in people with chronic schizophrenia. **Method**: Our sample was composed of 116 subjects with a schizophrenia diagnosis (evolution time = 17.5±9.5 years) from consecutive referrals to the Rehabilitation Unit of Benito Menni Hospital (Valladolid, Spain). All participants completed an extensive standardized protocol including a neuropsychological testing of executive functions (processing speed, working memory, inhibition, interference control, mental flexibility), the assessment of behavioral symptoms, and functional performance. Hierarchical regression models (HRMs) were carried out to determine whether education (in years) relates to executive functions after controlling for the effect of demographics, IQ, and clinical factors. **Results**: Both IQ and years of education were associated with a later onset of the illness. Specifically, high education (in years) significantly correlated with fewer behavioral problems and better functional performance in daily life. Further, HRMs showed that education was associated with digit span and sematic verbal fluency tasks after controlling for the effect of age, sex, and IQ as covariates. **Conclusions:** Higher education may ameliorate executive deficits in patients with chronic schizophrenia and, in turn, diminish the behavioral and functional problems of the illness.

Key Words: Education, Cognitive Reserve, Schizophrenia, Executive Functions; Psychological and Behavioral Symptoms.

Key points

1) Question: This research addresses the role of education, as cognitive reserve proxy, on cognitive, functional and behavioral outcomes in people with chronic schizophrenia.

2) Findings: Higher education is associated with less executive dysfunction, behavioral problems and better daily life functioning in individuals with chronic schizophrenia.

3) Importance: The engagement in cognitive stimulating activities may help people with chronic schizophrenia to cope better with manifestations of the illness.

4) Next Steps: Longitudinal studies combining behavioral and neuroimaging data are required to determine specific weights of different cognitive reserve proxies on the clinical course of schizophrenia.

Introduction

The concept of cognitive reserve (CR) originally refers to the ability to optimize task performance through recruitment of alternative neural networks (i.e., implying a more flexible and efficient use), and/or the use of different cognitive processes, which may help individuals actively offset the consequences of neuropathology (Stern, 2002). CR is primarily influenced by genetic and neurodevelopmental factors, but it may vary depending on certain variables such as education, lifestyle, and mental activities (Bora, 2015). This is possible due to brain plasticity, a term that refers to the brain's ability to adapt functionally and structurally in response to a constantly changing environment (Burke & Barnes, 2006). Thus, individuals with higher CR are less likely to develop dementia (Contador, Bermejo-Pareja, Puertas-Martín, & Benito-León, 2015; Stern et al., 1994), because they cope better with the clinical symptoms and manifestations of neuropathology (Scarmeas & Stern, 2004; Stern, 2013). Accordingly, some authors underline that CR may also explain individual differences in the expression of psychiatric disorders such as schizophrenia (Barnett, Salmond, Jones, & Sahakian, 2006). In this sense, CR may be important not only for reducing the risk of schizophrenia (Khandaker et al., 2011), but also to better understand the expression of symptoms and patients' functioning (Herrero, Contador, Stern, Fernández-Calvo, Sánchez, & Ramos, 2020).

It is known that schizophrenia is a complex and heterogeneous broad-spectrum disorder characterized by neurocognitive deficits (Heinrichs & Zakzanis, 1998; Rund et al., 2007). In particular, cognitive deficits can be moderate to severe across several domains, including attention, working memory, verbal learning, and memory, and executive functions (Bowie & Harvey, 2006). Most importantly, the presence of such deficits in patients with schizophrenia has been linked to worse worse functioning in everyday-life activities (Bowie, Reichenberg, Patterson, Heaton, & Harvey, 2006; Leeson, Barnes, Hutton, Ron, & Joyce, 2009; Robinson, Woerner, McMeniman, Mendelowitz, & Bilder, 2004) and severity of the symptoms (Lam, Raine, & Lee, 2014), even in phases of clinical remission (Bowie et al., 2006; Galderisi et al., 2014; Green, Kern, Braff, & Mintz, 2000). Further, it seems that cognition and, more specifically, executive functioning can influence the benefits of treatments due to the fact that impairments in the executive domains are usually associated with less engagement in therapy and medication compliance (Bowie & Harvey, 2006).

According to a recent systematic review, the effect of socio-behavioral CR proxies (i.e, IQ, education) in people with schizophrenia has usually been analyzed through cognitive outcomes, whereas studies on social or functional consequences are inexistent (Herrero et al., 2020). Robust scientific evidence has demonstrated the importance of education in preventing cognitive decline and dementia incidence in older populations (Meng & D'Arcy, 2012; Matyas et al 2019). However, the role of education in schizophrenic patients has mostly been analyzed in combination with other proxies such as premorbid IQ (Amoretti et al., 2018; de la Serna et al., 2013; Holthausen et al., 2002), so its specific effect on different schizophrenia outcomes has not been thoroughly investigated, and the current studies present difficulties in terms of methodology and data interpretation. For instance, Kanchanatawan et al. (2018) found that high education, taken as covariate (secondary analysis), was more common in simple forms of neurocognitive psychosis (a less well- developed phenotype), whereas Herold et al. (2019) described a negative association between education and neurological signs in chronic patients with schizophrenia. Finally, Ward et al. (2017) suggested that high and moderate levels of education (vs. low levels) may be protective factors against cognitive impairment in patients with schizophrenia, but this effect was restricted to individuals who were carriers of cardiovascular risk alleles (i.e., ACE D and APOE ε4).

It should also be considered that most of the studies on CR have been carried out after the first schizophrenic episode because cognitive and functional decline occur mainly before or during the onset of the disease (Kelly, Sharkey, Morrison, Allardyce, & McCreadie, 2000; Rabinowitz et al., 2000). However, Herold et al. (2019) reported that neurological signs and psychopathological symptoms (e.g., thought disturbances) of schizophrenia may also be associated with its chronicity. To support this observation, longitudinal MRI studies have shown an accelerated loss of gray matter over time in schizophrenia (Dietsche, Kircher & Falkenberg, 2017), which seems particularly pronounced in poor outcome patients (Mitelman et al., 2009ab). Consequently, it would be relevant to investigate the role of CR in moderating the impact of pathophysiological processes underlying brain changes in chronic stages of schizophrenia.

This research aimed to assess the specific effect of education on standardized cognitive, clinical, and functional variables in a large sample of chronic patients with schizophrenia. To our knowledge, this study provides new insights on the effect of CR in behavioral and functional outcomes of chronic schizophrenia, extending the traditional approach focused on cognitive outcomes (Herrero et al. 2020; Roldán-Tapia, Cánovas, León, & García-Garcia, 2012). According to CR expectations, a higher educational level should be associated with better cognitive-functional performance and fewer behavioral problems in chronic patients with schizophrenia. A hierarchical regression framework was used to control the influence of IQ, sociodemographic factors, and clinical variables on the mentioned associations. The current work could shed light on the specific impact of education, as a CR proxy, on different outcomes (cognitive, functional, and behavioral) in the chronic phase of schizophrenia.

2. Methods

2.1. Participants

A total of 116 patients who met diagnostic criteria for schizophrenia were recruited from consecutive referrals to the Rehabilitation Center of the Benito Menni Hospital (Valladolid, Northwest of Spain). Schizophrenia diagnosis was carried out according to the International Statistical Classification of Diseases, 10th Revision (World Health Organization, 1992). Each patient was diagnosed by a specialist in psychiatry based on a clinical interview (history and assessment of the mental state) with the patient and his or her family. All patients included in this study presented a clinical progression of symptoms of at least two years and were suffering from significant functional and social impairment. Subjects with concomitant organic illnesses or another psychiatric disease different from schizophrenia, history of substance abuse, presence of serious behavioral disorders (e.g., aggressive behavior), or an IQ lower than 70 were excluded from the study. All participants were volunteers and signed written informed consent, with the assistance of their legal tutor if necessary, before enrolment in the study. This research was approved by the hospital's ethics committee.

2.2. Measures

The comprehensive standardized protocol included the collection of sociodemographic variables (age and sex), CR proxies (years of education and occupation), clinical information (age at onset, duration, number of relapses, days of hospitalization), a measure of general intelligence, executive function testing, and evaluation of behavioral and functional problems. Occupation was evaluated based on the work type and complexity level, but this variable was not analyzed because many of the subjects evaluated had not performed any work. If they have done so, it was for very short periods of time before abandoning it. The evaluation tests of the standard protocol are described in detail below.

The Positive and Negative Syndrome Scale (Kay, Fiszbein, & Opler, 1987). The scale assesses the severity of symptomatology (positive and negative) and general psychopathology. It consists of 30 items; 7 for the positive scale, 7 for the negative scale, and 16 for the general psychopathology scale. All items are rated on a 7-point scale of severity (1 = absent; 7 = extreme)

The Global Assessment of Functioning (GAF; APA, 2001). This scale assesses the severity of the patient's mental illness on a scale ranging from 0 to 100. The lower the scores on this scale, the more difficulties in performing daily life activities.

The Kaufman Brief Intelligence Test (K-BIT; Kaufman, 2000). It measures the level of intelligence for ages between 4 and 90 years. The Vocabulary subtest assesses verbal skills related to school learning (crystallized intelligence), whereas the Matrices subtest assesses nonverbal skills and the ability to solve new problems (fluid intelligence). Overall (composite) IQ scores range from 40 to 160, with higher scores indicating a higher level of intelligence.

Perceptual-motor speed processing. This domain was assessed by the Digit Symbol-Coding and Symbol Searching subtasks of the Wechsler Adult Intelligence Scale-fourth edition (WAIS-IV; Wechsler et al., 2014). Symbol searching requires the examinee within 120 s whether a target symbol appears (yes vs. no) among the 5 symbols shown in a search group. Digit Symbol-Coding consists of transcribing numbers to symbols according to the legend provided. Each item is presented sequentially in a row, and the examinee has 120 s to pair specific numbers with given geometric figures.

Attention and working memory. This factor was assessed by the Digits Forward and Backwards subtasks of the WAIS-IV (Wechsler et al., 2014). It requires subjects to repeat a series of increasing numbers, which are presented orally. Starting with two, at a rate of one per second, numbers must be repeated in the forward or backward conditions. The test ends when two consecutive mistakes are made on each condition.

Verbal fluency test (Delis, Kramer, Kaplan, & Holdnack, 2004). Both conditions, semantic and phonological fluency, were applied. In the semantic task, participants were asked to name as many elements as they could in two semantic categories, animals and fruits. In the phonological condition, subjects were asked to say as many words as possible that begin with a particular letter (F, A, S). Time limit for both tasks was 60 seconds. Scores were based on the number of responses given for each condition.

Mental Flexibility and Inhibition. This components were tested y the Stroop Test (Golden, 1978) and the Trail Making Test (TMT; Reitan & Wolfson, 1985).

The Stroop Test (Golden, 1978) consists of three conditions: 1) list of words (black ink) that name colors (red, green, and blue), b) list of stimuli in the form of “x” (red, green, and blue); c) the interference condition in which the subject should name the color of the ink of the words that name colors (red, blue, and green). The stimuli are organized in columns and should be named as quickly as possible within 45 seconds. An interference measure was calculated based on the time needed to complete the first two subtasks in comparison with the time needed to complete the third subtask (Scarpina & Tagini, 2017).

The TMT consists of two parts (A and B).

Part A is the simplest and consists of connecting series of randomly arranged, numbered circles, in order, whereas part B requires alternating numbers and letters. For parts A and B, scoring is expressed in terms of the time required to complete the tasks.

The Health of the Nation Outcome Scale (HONOS; Wing, Curtis, & Beevor, 1996). This instrument was designed to measure physical, personal, and social problems in patients with mental illnesses using secondary or tertiary mental health services (Casas, Escandell, Ribas, & Ochoa, 2010). The scale is composed of 12 items divided into 4 subscales: Behavioral Problems (disruptive behavior, self-harm, and substance use), Impairment (cognitive problems and physical impairment), Clinical/Symptomatic Problems (depression, hallucinations and delusions, and other mental or behavioral problems), and Social Problems (problems with relationships, activities of daily living, living conditions, and occupation). Each item is scored on a five-point scale ranging from 0 to 4. The maximum score is 48, with higher scores indicating greater severity.

2.3. Procedure

Before enrollment, the aims of the study were explained, and each patient signed an informed consent form. All participants underwent a standardized evaluation protocol at the time of admission to the rehabilitation center. The protocol was applied by a clinical psychologist specialized in the management of patients with mental disorders. During the first interview, a preliminary talk was carried out with the patients and accompanying relatives to record basic sociodemographic information. Then, an exhaustive socio-medical history, with the help of reliable informants (relatives or legal tutors), was collected in order to gather information about diagnosis, age at onset, number of relapses, evolution, treatments, stays in other mental units, and socio-economic status. Finally, different standardized instruments were applied to assess participants' neuropsychological performance, behavioral and functional problems.

2.4. Data analysis

All data analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 21 for Mac. The descriptive analysis was conducted for the total sample, including mean and standard deviations ($M \pm SD$) for the quantitative variables. Frequencies and percentages were used for the nominal variables. Taking into account that atypical antipsychotics may have benefits on cognitive performance (see Guilera, Pino, Gómez-Benito, & Rojo, 2009), patients were stratified by antipsychotic medication (atypical/combined antipsychotics vs. typical antipsychotics) to explore potential differences between these groups on each measure.

Normality was tested in dependent variables using skewness and kurtosis statistics (Hair, Black, Babin, & Anderson, 2010). All outcomes were adjusted to a normal distribution except for symbol search, phonological fluency, and TMT-B, which did not conform to normality even after logarithmic transformation (x+1). As a general approach, Pearson's correlations were performed between education (in years) and different outcomes, whereas t-tests were used to compare mean differences for independent groups (typical vs. atypical antipsychotics). In addition, non-parametric test (Spearman's correlation test and the Mann–Whitney U-test) were applied to confirm the statistical significance for exceptional variables which did not comply with the assumption of normality. Alternatively, chi-squared was applied to compare differences in frequencies between categorical variables.

Finally, hierarchical multiple regression (HMRs) analyses were performed to examine the effect of education on executive tasks after controlling for age, sex, IQ, and main clinical factors such as age (onset), illness duration, and number of relapses. The coefficient of multiple determination for multiple regression (R^2) was evaluated in conjunction with residual plots (x = regression standardized predicted value, and y = regression standardized residual) in order to assess the goodness of fit of the regression model to the data and rule out potential biases. Detection of multicollinearity was performed using the Variance Inflation Factor (VIF), with VIF > 5 as cut-off point for the diagnosis of collinearity (Sheather, 2009). The significance threshold (alpha) adopted in all statistical analyses was set to 0.05.

3. Results

Characteristics of the sample.

Table 1 summarizes the sociodemographic and clinical characteristics of the sample, stratified by type of antipsychotic medication. Participants were middle-aged, men in a higher proportion (62%), with a medium level of education. Negative symptoms were more common than positive symptoms, and most of the patients were under treatment with atypical antipsychotics. As shown in Table 1, no differences emerged between typical/combined antipsychotics and atypical antipsychotics subgroups in clinical and sociodemographic factors. These groups were matched in terms of cognitive, functional, and behavioral measures, except for performance on the Digit Span task.

[INSERT TABLE 1]

Associations between education, IQ and target outcomes

Education (years) and IQ showed a moderate correlation (r = .499**, $p < .001$). Table 2 shows the correlations between education or IQ with different outcomes, including the clinical characteristics of the sample.

[INSERT TABLE 2]

Education and IQ were positively associated with age at onset, whereas both variables correlated negatively with the presence of positive psychotic symptoms. Furthermore, education and IQ showed significant positive correlations with working memory (Digit Span) and verbal fluency tasks (semantic and phonological), whereas IQ was associated with a wider range of cognitive outcomes, including inhibitory control (Stroop) and TMT-B. Finally, education, but not IQ, was negatively correlated with global functioning scores (GAF) and the Clinical Problems subscale (HONOS).

Influence of education and IQ on cognitive performance

Finally, hierarchical multiple linear regression (MLR) analyses were performed to calculate the amount of variance explained by IQ, after entering demographic variables (age, sex, and education), in the Digit Span and verbal fluency tasks —semantic and phonological.

In the first step, education was a significant predictor of Digit Span (b = .018, 95% CI [.012, .002], p = 0.01] and semantic verbal fluency performance (b = .024, 95% CI [.009, .038], p =0.01) after controlling the effect of age and sex. This effect did not reach statistical significance, but a marked tendency was also found in phonological fluency tasks (b = .018, 95% CI [-.001, .038], p =0.06). After the inclusion of IQ (second step), the effect of education remained significant for Digit Span and showed a marked trend toward significance on Semantic Fluency. Finally, when clinical covariates (age at onset, illness duration, and number of relapses) were included, the effect of education remained significant for semantic fluency (b = .021, 95% CI [003, .039], p = .02), but it was no longer significant for Digit Span (b = .003, 95% CI [-.013, .018], p = .73).

[INSERT TABLE 3]

4. Discussion

The main aim of this study was to analyze the specific influence of education, as CR proxy, on executive functions, behavioral symptomatology, and functional performance in chronic patients with schizophrenia. Our findings showed that higher education was specifically associated with better cognitive and functional performance and fewer clinical problems, including positive symptoms. In fact, previous observations suggest that education can potentially alleviate the cognitive manifestations in patients with chronic schizophrenia (Kanchanatawan et al., 2018; Ward et al., 2017). In this regard, education is a well-known CR proxy associated with the prevention of cognitive and functional decline (Matyas et al 2019; Meng & D'Arcy, 2012), although current evidence in people with schizophrenia is still scarce (see Herrero et al., 2020). Moreover, using HRMs, this study shows that higher education was associated with better performance on Digit Span and Semantic Verbal Fluency after controlling for the effects of sociodemographics and IQ. Consistently, de la Serna et al. (2013) showed that education improves the ability of IQ to predict cognitive performance in attention and working memory in people with schizophrenia.

Further, this study provides new insights on the effect of education on behavioral and functional outcomes of chronic schizophrenia. Other studies found that CR was also related to lower negative symptoms in patients with schizophrenia (Amoretti et al., 2016; Mäkinen et al., 2010), but such association was non-significant in our study. This heterogeneity might be due to CR's operationalization. For instance, Mäkinen et al. (2010) used school performance as a proxy of CR in their study, whereas Amoretti et al. (2016) applied a complex index of CR based on premorbid IQ, education, and leisure activities. In addition, it should be considered that only the effect of semantic fluency remained significant when clinical factors were included in the model and different interpretations may coexist in this regard. Firstly, education may have a higher effect on reducing the severity of cognitive problems after the first schizophrenic episode but, as the severity of the grey matter damage increases in chronic patients (Dietsche et al., 2007), the protective role of education decreases. Thus, CR—and specifically, education—may slow down cognitive and clinical deterioration, but its protective role gradually diminishes at long-term. Secondly, years of education may have a limited capacity to estimate CR in schizophrenic individuals with limited access to education, as occurs in other populations (Contador et al., 2015; Dotson, Kitner-Triolo, Evans & Zonderman, 2009). In fact, people with schizophrenia often leave school early.

Finally, HRMs are focused on the independent effect of education on the executive tasks eafter controlling for a wide range of covariates (IQ, demographics, and clinical characteristics).

The differential effect of education on executive tasks might illustrate the existence of complex relationships between them when different covariates are taken into account (e.g., age or severity of the illness).

This study has some limitations that should be pointed out. First, we presented herein a correlational cross-sectional study, which does not allow discriminating whether education is truly an indicator of CR or whether simply related to better cognitive performance. Indeed, education shows a robust association with the level of cognitive performance, but whether education is consistently associated with cognitive changes remains controversial (Seblova, Berggren & Lövdén, 2020). Further, the interpretation of these findings in terms of causality should be avoided. Schizophrenia is a multicausal entity of unknown etiology, possibly epigenetic, in which the interaction of genes and the environment promote disruptions in brain networks (Akbarian, 2014; Smigielski, Jagannath, Rössler, Walitza, & Grünblatt, 2020). In this context, our results suggest that CR may ameliorate cognitive-functional deterioration and behavioral symptoms, but direct causality between CR and schizophrenia emergence should not be inferred. Second, CR was estimated with education, as a single proxy of CR, so it is important to understand the specific weight of CR indicators (see Grotz, Seron, Van Wissen, & Adam, 2017), whose effects are usually overshadowed in complex CR indexes (see Amoretti et al., 2018; de la Serna et al., 2013). Finally, this study is focused on executive functions, so the results are not generalizable to other cognitive domains such as memory. One of the main strengths of this study is the diverse characteristics and the broad size of the sample. However, the generalization of these findings to the whole population of people with schizophrenia, a broad heterogeneous condition, should be done cautiously.

To sum up, our findings highlight that patients with a superior educational level would cope better with cognitive-functional problems and the severity of the clinical manifestations of the illness. Therefore, education might be an important factor for tailored interventions in people with schizophrenia, considering different evidences which suggest that effectiveness of cognitive intervention programs may be mediated by the influence of CR (Amoretti et al., 2018; Buonocore et al., 2019; Fiszdon, Choi, Bryson, & Bell, 2006). Otherwise, education may be associated with greater awareness of the disease (trans-diagnostic factor), increasing treatment adherence (Buckley, Wirshing, Bhushan, Pierre, Resnick, & Wirshing, 2007), which may result in less chronicity and severity of the symptoms. Future research should address the role of education and other CR proxies to optimize the benefits of intervention programs carried out in patients with schizophrenia at different levels of chronicity.

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Table 1. Characteristics of the sample: comparisons between patients with typical versus atypical antipsychotic drugs.

Variables	Total sample (*n* = 116)	Typical or combined (typical plus atypical) intervention (*n* = 33)	Atypical antipsychotics only (*n* = 83)	*p*
Age	40.66 (9.62)	42.64 (9.03)	39.98 (9.78)	.151
Sex (n, % male)	73 (62.90)	24 (72.7)	49 (59)	
Education (years)	13.84 (3.93)	13.97 (3.44)	13.80 (4.12)	.817
K-BIT (IQ)	90.16 (11.64)	89.36 (11.26)	90.47 (11.85)	.640
Age at onset (years)	23.03 (5.95)	23.94 (5.23)	22.67 (6.21)	.270
Duration (years)	17.54 (9.58)	18.09 (10.69)	17.33 (9.16)	.719
Hospital admittance (days)	493.11(284.6)	533 (236.6)	477.01(301.4)	.289
Relapses (n)	2.93 (3.42)	2.64 (3.73)	3.05 (3.13)	.582
Positive symptoms (PANSS)	14.84 (5.09)	14.85 (4.65)	14.84 (5.29)	.996
Negative symptoms (PANSS)	22.74 (9.10)	23.48(10.80)	22.45 (8.40)	.622
Other Medications				
Anxiolytics (n, %)	70 (60.3)	54 (48.5)	54 (65.1)	.227
Antidepressants (n, %)	34 (29.3)	12 (26.4)	22 (26.5)	.154
Mood stabilizers (n, %)	16 (13.8)	3 (9.1)	13 (15.7)	.367
Anti-Parkinsonism (n, %)	102 (12.1)	6 (17.7)	8 (9.6)	.234
Cognitive Testing				
Digit Symbol Coding	50.25 (14.36)	50.06(16.74)	50.32 (13.41)	.936
Symbol Search	23.50 (6.32)	23.48 (7.23)	23.50 (5.97)	.988
Digit Span[Ṫ]	12.30 (3.71)	13.82 (5.32)	11.70 (2.65)	.035*
Phonological Fluency	9.80 (3.21)	9.27 (3.28)	10.01 (3.18)	.274
Semantic Fluency	14.68 (4.30)	14.88 (4.40)	14.60 (4.29)	.760
Stroop (interference)	-1.65 (10.43)	-3.84(11.49)	-.77 (10.27)	.163
TMT B (seconds)	142.48 (66.0)	147.85(76.1)	140.35 (61.9)	.617
GAF	52.73 (10.32)	53.21(11.29)	52.14 (9.92)	.362
HoNOS	13.12 (13.00)	12.85 (4.65)	13.23 (4.19)	.684
Behavioral problems	1.24 (1.42)	.97 (1.35)	1.35 (1.44)	.187
Impairment	1.88 (1.42)	1.67 (1.38)	1.96 (1.43)	.306
Clinical Problems	3.89 (1.95)	5.06 (2.26)	3.82 (1.83)	.588
Social Problems	6.08 (2.61)	5.94 (2.67)	6.13 (2.60)	.725

Numbers represent means and standard deviations (between parentheses) for quantitative variables. PANSS. Positive and Negative Symptoms Scale; HONOS. Health of the Nation Outcome Scale; GAF. Global Assessment Functioning; K-BIT = The Kaufman Brief Intelligence test; IQ = Intelligence quotient;
Ṫ = sum of forward and backward condition; **p* < .05.

Table 2. Correlations between education and IQ with cognitive, behavioral, and functional outcomes.

	Education (years)	IQ
Clinical Factors		
Age at onset (years)	.352**	.252**
Duration (years)	-.123	.026
Hospitalization (days)	.158	-.096
Relapses (n)	-.059	-.119
Positive symptoms (PANSS)	-.304**	-.262**
Negative symptoms (PANSS)	.051	-.045
Neuropsychological Testing		
Digit Symbol Coding	.081	.013
Symbol Search[¥]	.176	-.032
Digit Span	.211*	.297**
Semantic Verbal Fluency	.327**	.295**
Phonological Verbal Fluency[¥]	.224*	394**
Stroop Word-Color (interference)	-.162	-.215*
TMT-B (seconds)[¥]	-.156	-.254**
Global Assessment Functioning (GAF)	.201*	.162
HONOS	-.122	-.069
Behavioral problems	-.081	-.189
Impairment	.143	-.043
Clinical problems	-.208*	-.060
Social problems	-.006	-.097

**p* < .05. ***p* < .01.

[¥] Pearson correlations were non-significant for these variables. Non-parametric correlations are shown.

Table 3. Hierarchical regression models examining the effect of education and intelligence quotient (IQ) on cognitive measures.

	Intercept	*b*	95% CI	*p*
Digit Span				
Model. R^2 = .187, F = 6.384, p < .001	2,953			
Age		-.008	-.014, -.003	-.008
Sex		-.011	-.119, .096	-.011
Education		.005	-.010, .020	.005
IQ		.009	.004, .014	.009
Semantic Verbal Fluency				
Model. R^2 = .142, F = 4.608, p = .002	2,879			
Age		002	-.004, .008	.445
Sex		.060	-.059, .180	.318
Education		.017	.000, .034	.054
IQ		.005	-.001, .010	.101
Phonological Fluency				
Model. R^2 =.154, F = 5.053, p = .001	2,229			
Age		-.006	-.013, .001	.117
Sex		.024	-.126, .175	.748
Education		-.002	-.024, .019	.834
IQ		.014	.007, .021	.001

Note. b = unstandardized Beta Coefficient. Residual plots were randomly dispersed around the horizontal axis, supporting the appropriateness of the linear regression model to the data. All VIF values fell below the cut-off point of 5.